Choosing an SSRI in Major Depressive Disorder

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Case 1

- 48 yo Female
- CC – f/u St. Joseph Urgent Care neck pain
  - Long history of untreated depression, has decided to start treatment, wants something that won’t make her too tired or gain weight.
- PMH
  - Pain: claims to have migraines and “fibromyalgia”
  - UTI
  - Has partnership health plan
- Current medications
  - Hydroxyzine HCl 10mg 1-2T PO Q6 for anxiety
  - Albuterol 90 mcg/act Inhaler Inhale 2 puffs Q4-6
  - Ibuprofen 600mg 1T PO Q4-6 prn.
  - Flonase 50mcg/act Inhaler Inhale 2 sprays in each nostril daily
  - Prilosec OTC 20mg 1T PO daily
  - Vicodin 5/500mg 1T PO Q8 prn for severe pain
  - Oxybutynin Chloride 5mg 3T PO up to three times daily

Demographics

- 300 million people affected by Depression world wide
- Women more commonly than men
  - 15-20% of Women
  - 7-12% of Men
- 16.2% Lifetime prevalence
- 51.6% Patients with MDD receiving treatment
- 41.9% Patients with MDD receiving adequate treatment

Pathophysiology

- Biogenic Amine Hypothesis
  - Depression caused by decrease in neurotransmitters in the synaptic cleft
    - Serotonin
    - Norepinephrine
    - Dopamine
  - Several other theories...

SSRI Mechanism of Action

SSRIs

- Fluoxetine (Prozac)
- Paroxetine (Paxil)
- Citalopram (Celexa)
- Sertraline (Zoloft)
- Escitalopram (Lexapro)
Other treatments

- SNRI (Serotonin and Norepinephrine Reuptake Inhibitors)
  - Duloxetine (Cymbalta)
  - Venlafaxine (Effexor)
- TCA (Tricyclic Antidepressant)
  - Amitriptyline
  - Nortriptyline
- Others
  - Bupropion (Wellbutrin)
  - Mirtazapine (Remeron)

Treatment Goals

- Goal of treatment is remission (absence of symptoms) instead of response (>50% decline in depression score)
- 33% of patients achieve remission

Comparative Efficacy

- SSRIs are relatively effective compared with SNRIs, Mirtazapine, and Bupropion for first line treatment
  - Most effective
    - Mirtazapine, escitalopram, venlafaxine, and sertraline
  - Best Tolerated
    - Escitalopram, sertraline, citalopram, and bupropion.

How to choose?

- Medication history
- Safety in overdose
- Tolerability of side effects
- Drug Interactions
- Symptoms
- What does the patient prefer?

SSRI
Early discontinuation of Treatment due to Adverse Events

- ~5% of fluoxetine
- 6% to 8% of escitalopram
- 9.4% to 20% of paroxetine
- 10% to 15% of sertraline
- 16% of citalopram

SSRI Side Effects
CNS

- Most Activating to most sedating
  - Fluoxetine
  - Sertraline
  - Escitalopram
  - Citalopram
  - Paroxetine

### SSRI Side Effects

#### GI
- Generally resolve in the first few weeks.
  - Constipation
    - Paroxetine 16%
    - Citalopram 13%
  - Nausea
    - Fluoxetine 20-30%
    - Paroxetine 26%
    - Citalopram 20-21%
    - Escitalopram 15-18%
    - Sertraline 13-30%
  - Diarrhea
    - Paroxetine 18%
    - Sertraline 13-14%
    - Escitalopram 6-14%

### SSRI Side Effects

#### Sexual Dysfunction
- Depression can cause decreased libido
- SSRI can cause orgasm problems (delayed)
  - Treatment
    - Switch antidepressants to bupropion or mirtazapine
    - Lower the SSRI dose

### SSRI Side Effects

#### Sweating
- Tooth grinding
- Weight gain (paroxetine the most)
- SIADH
- Withdrawal
- GI bleeds

### SSRI Citalopram QT Prolongation
- 2011, The FDA added a warning to Citalopram
  - Not to exceed 40mg in healthy patients
  - Not to exceed 20mg in older patients and when taking medications that can increase Citalopram concentration or that also increase QT interval.
  - Citalopram is metabolized by CYP 2C19
    - Drugs that inhibit CYP 2C19 can increase Citalopram concentration
      - Omeprazole
      - Cimetidine
  - Some medications that prolong QT interval
    - Methadone
    - Tricyclic Antidepressants
    - Fluoroquinolones
    - Macrolides
    - Antipsychotics (haloperidol, chlorpromazine, ziprasidone)
    - Antiarhythmic

### SSRI Citalopram QT Prolongation
- Is the QT prolongation clinically significant?
  - QT interval and antidepressant use: A cross sectional study of electronic health records.
  - Comparison of toxicity of Acute Overdoses with Citalopram and Escitalopram
- How to monitor?
  - Baseline EKG
  - Electrolytes (especially K and Mg)
  - HR
  - Prescreening?
SSRI Drug Interactions

- **CYP2D6**
  - Inhibitors
    - Fluoxetine, Paroxetine (Bupropion, Duloxetine)
  - Substrates
    - Beta Blockers, Narcotics (codeine, hydrocodone, oxycodone, tramadol)

- **CYP3A4**
  - Inhibitors
    - Fluoxetine, Paroxetine, Citalopram, Sertraline, Escitalopram
  - Substrates
    - TCAs, Statins (ALS), Alprazolam, Trizolam, Sildenafil, Zolpidem, CCBs, Estrogens, Corticosteroids, PIs, and others

- **NSAIDs**
  - Increased risk of GI bleeds with SSRIs
  - Synergistic not additive


SSRI Drug Interactions

- **Serotonin Syndrome**
  - Can occur with any medications that increase serotonin in the synaptic cleft
  - Symptoms
    - diaphoresis, tachycardia, hyperthermia, hypertension, vomiting, and diarrhea

Bupropion

- Increases Norepinephrine and Dopamine
- May be preferred in patients that are more tired than worried.
- Less sexual dysfunction
- AE – Headache, seizures, rash, nausea
- CI – History of seizures, Bulimia
- CYP2D6 inhibitor

SSRI Prices (30 day supplies)

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<th>Brand</th>
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<th>Walmart S4</th>
<th>Target S4</th>
<th>Costco</th>
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<tr>
<td>Fluoxetine</td>
<td>$5</td>
<td>10, 20, 40mg</td>
<td>10mg $5.99, 20mg $7.21, 40mg $18.41</td>
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<tr>
<td>Sertraline</td>
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<tr>
<td>Paroxetine</td>
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<td>10, 20mg</td>
<td>*10, *20mg</td>
<td>10mg $5.90, 20mg $5.90, 30mg $14.68, 40mg $15.49</td>
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<tr>
<td>Citalopram</td>
<td>$5</td>
<td>20, 40mg</td>
<td>20, 40mg</td>
<td>10mg $5.69, 20mg $6.90, 40mg $6.90</td>
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<tr>
<td>Escitalopram</td>
<td>-</td>
<td>-</td>
<td>5mg $6.99, 10mg $6.99, 20mg $6.99</td>
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</table>

- PHP also includes
  - Bupropion $20
  - Bupropion XR $45
  - Bupropion XL $30
  - Venlafaxine XR $30
  - Amitriptyline $5
  - Nortriptyline $5

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  - Floxurin 50mg/act trihedral 2 sprays in each nostril daily
  - Pribose 0.5/50mg 1 tab PO Q8 prn for severe pain
  - Lisinopril 1mg 1 tab PO daily
  - Oxybutynin 5mg 1-2 tabs PO up to three times daily
Case 2

- 35 yo Male
- CC – Cholesterol, feeling depressed and fatigued, doesn’t want to get out of bed most days.
- HPI – as noted, needs refill for Metamucil. Occasionally feels bloated
- Current medications
  - Simvastatin 40mg 1T PO at bedtime
  - Tylenol w/ codeine #3 1 T Q8 prn for pain
  - Claritin 10mg 1T PO daily
  - Proctozone – HC 2.5% cream 1 apply to affected area
  - Allegra allergy 60mg 1T PO BID
  - Sumatriptan succinate 50mg 1T PO at onset of HA
  - Metamucil 10.9% Powder as directed daily
  - Voltaren Gel 1.0% apply to affected area BID
  - Losartan 50mg 1T PO daily